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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/654,994	09/05/2003	Mark W.J. Ferguson	39-288	6683

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EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/654,994	FERGUSON, MARK W.J.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-28* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1106*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 02/28/2007 has been entered. Claims 20–28 are pending. Claims 20–27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), to the extent that they are drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on 07/17/2006. Claims 20–22 and 24–28 are being examined to the extent that they are directed to or encompass the elected species activin.

Maintained Formal Matters, Objections, and/or Rejections:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20–22 and 24–27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues that:

> In rejecting the claims as lacking written description, the Examiner appears to contend that each and every stimulator of activin must be structurally defined. No basis is seen for such a requirement.

Applicant's arguments have been fully considered but they are not persuasive. The examiner did not make such a contention. If applicant perceived an appearance of such of a contention, then applicant has misperceived the rejection. The rejection was for a failure to describe the "stimulator of activin" genus and not for a failure to describe "each and every stimulator of activin."

Applicant argues that:

> The disclosure is replete with examples of activin stimulators defined structurally, functionally or both. In view of the description provided, it would have been clear that Applicant was in possession of the entirety, of the claimed invention at the time of filing.

Applicant's arguments have been fully considered but they are not persuasive. Whereas the instant specification provides a detailed description of reduced scarring and wound healing with activin, the instant specification does not provide a structural formula which is definitive of all activin stimulators. Whereas the instant specification may identify a functional property which is common to "a stimulator of activin," it does not identify those defining structural elements which provide the structural and functional properties of all such stimulators. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is indeterminate, one of skill in the art would reasonably conclude that the disclosure fails to describe the genus. Thus, applicant was not in possession of the genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20–22, 24–25 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Mitrani (U. S. Patent No. 5,753,612).

Applicant argues that:

It was a new and non-obvious finding on the part of Applicant that activin can be used to promote healing with reduced scarring. The effects of activin on scarring are dose dependent. That is, different doses have markedly different effects on scarring. The doses described in the present specification all have beneficial effects on scarring (when assessed either macroscopically or microscopically). The doses considered by Mitrani are far higher than those shown by Applicant to promote healing with reduced scarring. Instead, the doses suggested by Mitrani would actually increase scarring.

Mitrani suggests that activin should be used in a dose range of between 0.001 mg/kg and 50 mg/kg body weight. Preferred dose ranges of activin are stated to be between 0.01 mg/kg and 10 mg/kg body weight.

The studies described in the instant application utilized rats weighing between 200g and 250g. These were treated with one of three separate regimes:

i) three administrations, each of 2.5 ng;
ii) three administrations, each of 5 ng; or
iii) three administrations, each of l0 ng.

Thus, in the lowest dosing regime, a total of 7.5 ng of activin was administered per rat, and in the highest dosing regime, a total of 30 ng of activin was administered per rat. These totals, respectively, correspond to between 34.1 and 30 ng/kg body weight (depending on size of rat) and between 136.4 and 120 ng/kg body weight.

It can readily be seen that these doses are considerably lower than those suggested in Mitrani. The lowest dose considered by Mitrani corresponds to 1 μg/kg, and the lowest preferred dose to 10 μg/kg. In contrast, the highest dose shown by Applicant to reduce scarring is 0.136 μg/kg (about one eighth of the lowest suggested by Mitrani), and the lowest dose is only 0.03 μg/kg (just 3% of the lowest dose suggested by Mitrani). Clearly, the skilled person following the teachings of Mitrani would not have arrived at a scar-reducing dose of activin, as required by the instant invention.

Furthermore, doses in the range of those suggested by Mitrani have been shown to be pro-scarring, rather than anti-scarring.

By way of example, transgenic mice that over-express activin A in the basal epidermis (calculated to lead to between 20 and 150 ng activin/ml blood - Munz et al 1999) exhibit enhanced scarring in response to full thickness excisional wounds (unpublished data from Munz et al, and described in Wankell et al 2003, and Sulyok et al 2004).

Rats of 200 to 250g weight have an average blood volume of approximately 13.5 ml. Thus, rats treated with regime (iii) above can be expected to achieve a total accumulation of 2.22 ng activin/ml blood (based on administration of a total of activin 30 ng activin, and assuming no breakdown of activin). This figure (for the highest dose regime contemplated by Applicant) is approximately one tenth of the lowest value reported by Munz et al. in mice exhibiting increased scarring. In turn, the lowest concentration of activin reported by Munz et al (approximately ten times that established by regime (iii)) is generally comparable with that arising from the lowest dose considered by Mitrani (approximately eight times that established by regime (iii)).

In the light of the above, it can be seen that an artisan, following the teachings of Mitrani, would not have arrived at the subject matter of the present claims (e.g., use of activin in an amount sufficient to reduce scarring) but would, in fact, have been led to use amounts of activin that would increase scarring.

Applicant's arguments have been fully considered but they are not persuasive. The only evidence offered in support of the assertion that the effects of activin on scarring are dose dependent is applicant citing unpublished data from Munz et al., as described in Wankell et al. 2003, and Sulyok et al. 2004. However, none of Munz, Wankell, or Sulyok are of record. The examiner cannot consider evidence that is not of record. Furthermore, applicant's assertion is based on a comparison of the exogenous activin dose administered by Mitrani with a dose of endogenous activin administered in a transgenic mouse model that overexpresses activin A. However, there has been no direct comparison of the application of the doses of exogenous activin suggested by Mitrani with the doses of exogenous activin taught in the examples of the present application. Furthermore, the chronic overexpression of activin in a transgenic animal is

not comparable to a single administration or even a few administrations over several days simply because in the case of the former the administration is chronic. Thus, the doses administered are different. According to applicant, the effects of activin on scarring are dose dependent. Therefore, the argument that the doses considered by Mitrani are higher than those shown by Applicant to promote healing with reduced scarring is not persuasive. In the absence of evidence to the contrary, the dose considered by Mitrani is an amount of activin "sufficient to promote said healing so that said healing with reduced scarring is promoted."

Claims 20–22, 24–25 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by De Kretser (U. S. Patent No. 5,196,192).

Applicant argues that:

> The disclosure of De Kretser et al. is entirely silent as to doses of activin that are to be used. Given the lack of this teaching, and the dose dependency discussed above, De Kretser et al. cannot be viewed as being inherently anticipatory.

Applicant's arguments regarding the dose dependency of activin are not persuasive, as discussed above. Therefore, De Kretser must be viewed as inherently anticipatory.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20–21 and 26–27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitrani (U. S. Patent No. 5,753,612) as applied to claims 20–21 above, and further in view of Ferguson (WO 92/17206).

Claims 20–21 and 26–27 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Kretser (U. S. Patent No. 5,196,192) as applied to claims 20–21 above, and further in view of Ferguson (WO 92/17206).

Applicant argues that:

> The fundamental failings of Mitrani and De Kretser are detailed above. Nothing in Ferguson would have cured the deficiencies of the primary references. Further, the Examiner is reminded that subject matter that is allegedly inherent cannot be relied upon in rejecting claims as obviousness.

Applicant's arguments have been fully considered but they are not persuasive. As discussed above, the dose considered by Mitrani is an amount of activin "sufficient to promote said healing so that said healing with reduced scarring is promoted," and De Kretser must be viewed as inherently anticipatory. Furthermore, De Kretser must be viewed as inherently anticipatory with respect to the administration of activin the results thereof. The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness. See M.P.E.P. 2112.

New Formal Matters, Objections, and/or Rejections:

Information Disclosure Statement

The information disclosure statement filed 11/09/2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the

content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the non-English language information referred to therein has not been considered.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 15, 2007